UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/674,722	06/27/2001	Alastair David Griffiths Lawson	1300-1-007	4141

23565 7590 06/01/2006

KLAUBER & JACKSON
411 HACKENSACK AVENUE
HACKENSACK, NJ 07601

EXAMINER
DIBRINO, MARIANNE NMN

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 06/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/674,722	LAWSON ET AL.	
	Examiner	Art Unit	
	DiBrino Marianne	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *34-38* is/are pending in the application.

4a) Of the above claim(s) *42 and 43* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *34-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3/29/03*.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. *attached hereto* .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment filed 3/29/06 is acknowledged and has been entered.

2. Newly submitted claims 42 and 43 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

The host cell recited in claim 42 and the method for making the host cell recited in claim 43 belong to non-elected Group III (originally claims 40 and 41, drawn to an effector cell containing a nucleic acid sequence encoding a chimeric receptor). The only "host cells" disclosed in the instant specification are effector cells that have nucleic acid molecules encoding the chimeric receptor introduced into them.

Since Applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 42 and 43 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP.

Claims 34-38 are presently being examined.

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 34-38 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification does not provide adequate written description of the claimed invention. The legal standard for sufficiency of a patent's (or a specification's) written description is whether that description "reasonably conveys to the artisan that the inventor had possession at that time of the. . .claimed subject matter", Vas-Cath, Inc. V. Mahurkar, 19 USPQ2d 1111 (Fed. Cir. 1991). In the instant case, the specification does not convey to the artisan that the Applicant had possession at the time of invention of the claimed nucleic acid sequence encoding a chimeric receptor, wherein the chimeric receptor contains two independent polypeptide chains recited in instant base claim 34, and wherein the spacer domain is from any polypeptide, the transmembrane domain is of any oligopeptide or polypeptide derived from all or part of a human CD4 transmembrane domain, wherein the intracellular domain is a signaling domain comprised of any naturally occurring polypeptide signaling sequence that is all or part of

the human CD4 intracellular signaling domain or the human TCR zeta chain and the antibody heavy chain variable region and the antibody light chain variable region do not come from the same antibody and/or do not have the same specificity.

The instant claims encompass a nucleic acid molecule that encodes a chimeric receptor wherein the two polypeptide chains are part of a single chain construct, and wherein the spacer domain is *any* sequence of amino acid residues *comprising* 20-100 amino acid residues, *i.e,* any sequence of any length, and the transmembrane domain is an amino acid sequence that *is derived from* all or part of a human CD4 transmembrane domain, *i.e,* it can contain portions of the human CD4 transmembrane domain with other undisclosed flanking and internal sequences, and the intracellular signaling domain comprises any naturally occurring polypeptide signaling sequence that is all or part of the human CD4 intracellular signaling domain or the human TCR zeta chain, *i.e,* it can contain other undisclosed flanking sequence unrelated to a human CD4 intracellular signaling domain or a human TCR zeta chain signaling domain, and wherein the chimeric receptor is unable to incorporate into a host cell and signal, or wherein the spacer and/*or* transmembrane domains of the first and second polypeptide chains are selected to remain unassociated, but the two said polypeptide chains do not remain unassociated and signal constitutively, and wherein the variable heavy and light chain regions may possess different antigen specificity and do not come from the same antibody.

The specification discloses that plasmids containing nucleic acid molecules, *i.e,* two nucleic acid molecules each encoding one polypeptide chain that make up the chimeric receptor may be transfected into Jurkat cells and the resulting transfected Jurkat cells produce IL-2 in the presence of CD33 positive HL60 target cells *in vitro* (especially page 14 at lines 32-36, abstract and pages 15-16). The specification further discloses that for *ex vivo* use, the DNA may be introduced into effector cells removed from the target host, such cells being CTL, TIL, NK, neutrophils, basophils, TH cells, dendritic cells, B cells haematopoietic stem cells, macrophages, or monocytes, *i.e.,* hematopoietic lineage cells (page 9 at lines 6-21). The specification discloses that a spacer may be any oligo or polypeptide serving to link the association and transmembrain domains of each chain, they may be derived from all or part of naturally occurring molecules such as from all or part of the extracellular region of CD8, CD4 or CD28 or an antibody constant region, including the hinge region, or natural spacing components between functional parts of intracellular signaling molecules, such as spacers between ITAMS, or may be a non-naturally occurring sequence. The specification discloses that the spacer and or transmembrane domains may be modified to reduce association (page 6 at lines 28-36 and page 7 at lines 1-15). The specification discloses that transmembrane domains may be any oligo- or poly-peptide and may be derived from a wide variety of sources such as all or part of the alpha, beta or zeta chains of the TCR, CD28, CD8, CD4, CD3 epsilon, CD45 and members of the tetraspan family (paragraph spanning pages 5-6).

One of skill in the art would not have recognized that Applicant was in possession of the necessary common attributes or features possessed by the members of the genus.

5. Claims 34-38 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not disclose how to make and/or use the instant invention, a nucleic acid sequence encoding a chimeric receptor containing two independent polypeptide chains, one chain comprising a VH extracellular ligand association domain, *i.e.*, an antigen binding region of VH, a spacer domain including from CD8, a transmembrane domain from all or part of human CD4 transmembrane domain and an intracellular domain that is a signaling domain comprised of any naturally occurring polypeptide signaling sequence that is all or part of the human CD4 intracellular signaling domain, the other chain comprising a VL antigen binding region domain, a spacer domain including from CD8, a transmembrane domain that is all or part of human CD4 transmembrane domain and TCR zeta chain signaling domain or a part of said domain, and wherein the chimeric receptor is in association with a carrier that is a viral, liposomal or plasmid vector, a cationic lipid or an antibody, and wherein the two chains of the chimeric receptor do not associate except in the presence of bound ligand.

The specification has not enabled the breadth of the claimed invention because the claims encompass a nucleic acid molecule that encodes a chimeric receptor wherein the two polypeptide chains are part of a single chain construct, and wherein the spacer domain is *any* sequence of amino acid residues *comprising* 20-100 amino acid residues, *i.e,* any sequence of any length, and the transmembrane domain is an amino acid sequence that *is derived from* all or part of a human CD4 transmembrane domain, *i.e,* it can contain portions of the human CD4 transmembrane domain with other undisclosed flanking and internal sequences, and the intracellular signaling domain comprises any naturally occurring polypeptide signaling sequence that is all or part of the human CD4 intracellular signaling domain or the human TCR zeta chain, *i.e,* it can contain other undisclosed flanking sequence unrelated to a human CD4 intracellular signaling domain or a human TCR zeta chain signaling domain, and wherein the chimeric receptor is unable to incorporate into a host cell and signal, or wherein the spacer and/*or* transmembrane domains of the first and second polypeptide chains are selected to remain unassociated, but the two said polypeptide chains do not remain unassociated and signal constitutively, and wherein the variable heavy chain region and the variable light chain region are not from the same antibody and/or do not possess the same specificity for the same antigen.

The specification discloses that plasmids containing nucleic acid molecules, *i.e,* two nucleic acid molecules each encoding one polypeptide chain that make up the chimeric receptor may be transfected into Jurkat cells and the resulting transfected Jurkat cells produce IL-2 in the presence of CD33 positive HL60 target cells *in vitro* (especially page 14 at lines 32-36, abstract and pages 15-16). The specification further discloses that for *ex vivo* use, the DNA may be introduced into effector cells removed from the target host, such cells being CTL, TIL, NK, neutrophils, basophils, TH cells, dendritic cells, B cells haematopoietic stem cells, macrophages, or monocytes, *i.e.,* hematopoietic lineage cells (page 9 at lines 6-21). The specification discloses that a spacer may be any oligo or polypeptide serving to link the association and transmembrain domains of each chain, they may be derived from all or part of naturally occurring molecules such as from all or part of the extracellular region of CD8, CD4 or CD28 or an antibody constant region, including the hinge region, or natural spacing components between functional parts of intracellular signaling molecules, such as spacers between ITAMS, or may be a non-naturally occurring sequence. The specification discloses that the spacer and or transmembrane domains may be modified to reduce association (page 6 at lines 28-36 and page 7 at lines 1-15). The specification discloses that transmembrane domains may be any oligo- or poly-peptide and may be derived from a wide variety of sources such as all or part of the alpha, beta or zeta chains of the TCR, CD28, CD8, CD4, CD3 epsilon, CD45 and members of the tetraspan family (paragraph spanning pages 5-6).

Evidentiary reference WO 95/02686 A1 (of record) teaches that it is not clear how a simple physical event such as aggregation results in a clearly distinguished physiological signal, and that engagement of cellular effector programs mediated by the T cell and B cell antigen receptors can be mimicked by cross-linking chimeric proteins bearing the intracellular domains of individual chains of the receptor complexes (page 7 at lines 9-21).

There is insufficient guidance in the specification as to how make and/or use the instant invention. Undue experimentation would be required of one skilled in the art to practice the instant invention. See In re Wands 8 USPQ2d 1400 (CAFC 1988).

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

7. Claims 35-38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claim 35 is indefinite in the recitation of "The nucleic acid sequence...in association with..." because it is not clear what is meant, *i.e.,* if the product is a composition comprising a nucleic acid sequence...in association with a carrier.

b. Claim 38 is indefinite in the recitation of "wherein the nucleic acid sequence is on a plasmid" because it is not clear what is meant, *i.e.,* if the product is a plasmid comprising the nucleic acid sequence of claim 34.

8. No claim is allowed.

9. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Marianne DiBrino whose telephone number is 571-272-0842. The Examiner can normally be reached on Monday, Tuesday, Thursday and Friday.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Christina Y. Chan, can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Marianne DiBrino, Ph.D.
Patent Examiner
Group 1640
Technology Center 1600
May 19, 2006

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600